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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 04/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/528,361	PETERS ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-32 are pending in the application.

Priority

1. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(**e**), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim

filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

The applicants' included a reference to their foreign priority document filed under 35 U.S.C. § 119(a).

Specification

2. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 23-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of claims 24-32 are not adequately enabled solely based on the modulation of the activity of a cholinergic receptors and/or monoamine receptors provided in the specification. Claims 24-32 are the method for treating any and all diseases and/or conditions associated with cholinergic receptor and/or monoamine

receptor, which are not remotely enabled. The scope of claims 24-32 includes diseases and/or conditions not even known at this time, which may be associated with cholinergic receptor and/or monoamine receptor. While the treatment of schizophrenia has been linked with cholinergic receptor and/or monoamine receptor inhibition the art does not recognize use of such inhibitors as broad based drugs for treating all disorders instantly embraced. Additionally, instant claim language embraces disorders not only for treatment but also for the prevention, which is not remotely enabled.

In addition, claims 25, 29 and 30 embrace any and all central nervous system, neurodegenerative disorders and inflammatory disorders, respectively. The scope of the method claims are not adequately enabled solely based on the inhibition of the cholinergic receptor and/or monoamine receptor provided in the specification.

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1, 3-5, and claims dependent thereon are vague and indefinite in that it is not known what is meant by "derivative" which implies more than what is positively recited. "Compound" is suggested.

b) Regarding claims 12, 13, 15, 17-19 and 21, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

c) Claim 14 is vague and indefinite in that it is not known what is meant by 1,2,3-oxa**dizol**-4-yl in the last species on page 7 and the first two species on page 8.

d) Claim 17 is vague and indefinite in that it is not known what is meant by the definition of the optionally substituted bicyclic aromatic heterocyclic group, which is not stated as a proper Markush grouping.

e) Claim 19 recites the limitation "acridinyl" in the definition of the polycyclic aromatic heterocyclic group. There is insufficient antecedent basis for this limitation in the claim.

f) Claim 20 recites the limitation "1-Methyl-2-indolyl" in the nomenclature of the 2nd species on page 14. There is insufficient antecedent basis for this limitation in the claim.

g) Claim 20 is vague and indefinite in that it is not known what is meant by 7-phtalazinolinyl in the 6th species on page 14.

h) Claim 20 recites the limitation "2-acridinyl" in the nomenclature of the 11th species on page 14. There is insufficient antecedent basis for this limitation in the claim.

i) Claim 20 recites the limitation "3-acridinyl" in the nomenclature of the 11th species on page 14. There is insufficient antecedent basis for this limitation in the claim.

j) Claim 21 recites the limitation "benzothienyl, benzofuryl, quinolinyl, isoquinolinyl, cinnolinyl, indolizinyl, indolyl, benzimidazolyl, benzothiazolyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, acridinyl, dibenzofuryl, dibenzothienyl, phenoxazinyl" in the definition of the optionally substituted aromatic monocyclic heterocyclic group of Ar. There is insufficient antecedent basis for this limitation in the claim.

k) Claim 22 recites the limitation "benzothienyl " in the nomenclature of the first four species on page 15. There is insufficient antecedent basis for this limitation in the claim.

l) Claim 22 recites the limitation "benzofuryl" in the nomenclature of the 5th – 8th species on page 15. There is insufficient antecedent basis for this limitation in the claim.

m) Claim 22 recites the limitation "quinolinyl" in the nomenclature of the 9th and 10th species on page 15. There is insufficient antecedent basis for this limitation in the claim.

n) Claim 22 recites the limitation "isoquinolinyl" in the nomenclature of the 11th species on page 15. There is insufficient antecedent basis for this limitation in the claim.

o) Claim 22 recites the limitation "cinnolinyl" in the nomenclature of the 12th species on page 15. There is insufficient antecedent basis for this limitation in the claim.

q) Claim 22 recites the limitation "indolizinyl" in the nomenclature of the 13th species on page 15. There is insufficient antecedent basis for this limitation in the claim.

r) Claim 22 recites the limitation "indolyl" in the nomenclature of the 14th species on page 15 and the 1st species on page 16. There is insufficient antecedent basis for this limitation in the claim.

s) Claim 21 recites the limitation "benzimidazolyl" in the nomenclature of the 2nd and 3rd species on page 16. There is insufficient antecedent basis for this limitation in the claim.

t) Claim 22 recites the limitation "benzothiazolyl" in the nomenclature of the 4th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

u) Claim 22 recites the limitation "phtalazinolinyl" in the nomenclature of the 5th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

v) Claim 22 is vague and indefinite in that it is not known what is meant by phtalazinolinyl in the 5th species on page 16.

w) Claim 22 recites the limitation "quinazolinyl" in the nomenclature of the 6th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

x) Claim 22 recites the limitation "quinoxalinyl" in the nomenclature of the 7th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

y) Claim 22 recites the limitation "naphthyridinyl" in the nomenclature of the 8th and 9th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

z) Claim 22 recites the limitation "acridinyl" in the nomenclature of the 10th and 11th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

aa) Claim 22 recites the limitation "dibenzofuryl" in the nomenclature of the 12th and 13th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

ab) Claim 22 recites the limitation "dibenzothienyl" in the nomenclature of the 14th and 15th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

ac) Claim 22 recites the limitation "phenoxazinyl" in the nomenclature of the 16th and 17th species on page 16. There is insufficient antecedent basis for this limitation in the claim.

ad) Regarding claims 26, 28, 30 and 32, the phrase "such as" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

ae) Claims 24, 25, 29 and 30 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by the modulation of cholinergic receptors and/or monoamine receptors. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a

drug, particularly in anti-inflammatories or neurodegenerative diseases, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

> only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, 6-8, 10-14, 17 and 23-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Galli et al., U.S. 6,998,399. Galli teaches the compounds, compositions and method of use of the compounds of formula I where n is 2, X is S and Ar is optionally substituted phenyl as set forth in the Table.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4, 6-8, 10-14, 17, 18 and 23-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galli et al., U.S. 6,998,399. The generic structure of Galli encompasses the instantly claimed compounds (see the formula I) as claimed herein. Examples set forth in the table, which anticipates the compounds, compositions and method of use of the compounds of formula I of the instant invention, differs only in the substituent R. Column 1, lines 28-41, defines the substiuents of the 4-(1,3,4-thiadiazol-2-yl)-1,4-diazabicyclo[3.2.2]nonane as follows: R represents a (C_3-C_6)cycloalkyl or a phenyl group optionally substituted with one or more groups chosen from a halogen atom, a (C_1-C_6)alkyl, (C_1-C_6)alkoxy, nitro, amino, di(C_1-C_3)alkylamino, trifluoromethoxy, trifluoromethyl, cyano, hydroxyl or methylenedioxy group or a 1-piperidinyl, 4-morpholinyl, 1-pyrrolidinyl, 1-azetidinyl, 1-azepinyl, pyridyl, thienyl, pyrazinyl, furyl,

benzofuryl, benzothienyl, indolyl, pyrimidinyl, isoxazolyl, phenoxazinyl, phenoxathiinyl, dibenzofuryl, dibenzothienyl, pyrrolyl or naphthyl, each of these groups possibly being substituted with one or more groups chosen from a halogen atom and a $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, trifluoromethoxy, trifluoromethyl, nitro, cyano, hydroxyl, amino, di$(C_1$-$C_3)$alkylamino or $(C_3$-$C_8)$cycloalkylamino group. The compounds, compositions and method of use of the compounds of formula (I) of the instant invention are generically embraced by Lochead in view of the interchangeability of the substitutions of the 1,4-diazabicyclo[3.2.2]nonane compounds. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example a imidazolyl, etc. as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brenda Coleman

Brenda L. Coleman
Primary Examiner Art Unit 1624
April 11, 2006